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Docket No.: K21364USWO (C038435/0184371)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :)
Werner BONRATH *et al.*) Examiner: Kellette Gale
Serial No.: 10/524,762) Art Unit: 1621
Filed: February 15, 2005)
For: ETHYNYLATION PROCESS)

DECLARATION OF DR. WERNER BONRATH UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O.Box 1450
Alexandria, VA 22313-1450

Sir:

I, Werner Bonrath, a citizen and resident of Germany, hereby declare as follows:

1. I studied chemistry at the Universities of Bonn and Münster, Germany from 1979 to 1985.
2. I received a doctorate in Chemistry in 1988 from the Max Planck Institute of Carbon Research, Mülheim an der Ruhr, Germany.
3. In 1988-1989, I was a post-doctoral fellow at the University of Innsbruck, Austria.
4. Since 1989, I have been employed at DSM Nutritional Products, B.V. (previously Roche Vitamins Ltd. and F. Hoffmann-La Roche Ltd.), Basel, Switzerland as a chemist in the research and development department for vitamins and fine chemicals.

5. I am one of the inventors of the invention described and claimed in the captioned application directed to an "ETHYNYLATION PROCESS".

6. The present application discloses and claims a process for the manufacture of an acetylenically-unsaturated alcohol. The reaction comprises reacting a carbonyl compound, selected from methyl ethyl ketone, methylglyoxal dimethylacetal, 6-methyl-5-hepten-2-one, 6-methyl-5-octen-2-one, hexahydropseudoionone, 4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-3-buten-2-one, and 6,10,14-trimethyl-2-pentadecanone, with acetylene in the presence of ammonia in a liquefied state, and an alkali metal hydroxide. The alkali metal hydroxide is used in aqueous solution, making it easier to handle and work with, and the molar ratio of the alkali metal hydroxide to the carbonyl compound is less than 1:200.

7. Under my supervision and direction, five comparative ethynylation reactions using different carbonyl compounds, described below, were performed. These experiments demonstrated that the claimed process using molar ratios of the alkali metal hydroxide to the carbonyl compound of less than 1:200 produced less than 50% of an unwanted diol by-product compared to processes using molar ratios greater than 1:200, which would not have been expected or predicted by one of ordinary skill in this art at the time the Application was filed.

8. The five ethynylation reactions were carried out as follows: potassium hydroxide ("KOH"), in a 45% (wt./vol.) aqueous solution, and the starting carbonyl ("SC"), in the molar ratios provided below ("KOH:SC") were introduced into a 2-liter

autoclave reaction vessel. Except in one case, for each carbonyl compound, three ethynylation reactions were carried out. One reaction wherein the molar ratio of the alkali metal hydroxide-to-carbonyl compound was above that in our process (but within the scope disclosed in the Tedeschi *et al* reference [U.S. Patent 3,709,946]) and, except in the same one case, two reactions wherein the molar ratio of the alkali metal hydroxide to carbonyl compound within the scope of our invention.

9. For each ethynylation reaction, the atmosphere in the reaction vessel was rendered inert by evacuating the air from it and flushing with nitrogen. 369 grams ammonia were then introduced into the reaction vessel. Acetylene was then added to provide a fixed total pressure at 30°C, corresponding to about 21% (wt./wt.) for each reaction. The duration of the reaction was either 1 or 2 hours and the temperature was maintained at 30°C throughout each reaction.

10. At the end of the reaction, the ammonia was evaporated off and the residue in the reaction vessel was acidified with 8% sulphuric acid and washed with water at 60°C, while maintaining the pH at 7. The percent conversion of the starting carbonyl into the acetylenically unsaturated alcohol product was determined by gas chromatography. The percentage yield of the product and the percentage yield of the unwanted diol by-product were then determined based on the percent conversion of the product.

11. As shown in my Declaration of October 1, 2007, submitted to the United States Patent and Trademark Office on October 3, 2007 (wherein the results of the above-described reactions were presented in table form), the use of potassium

hydroxide ("KOH", the alkali metal hydroxide)-to-various starting carbonyls (SC's) in a molar ratio of less than 1:200 (respectively, in molar amounts: 1 KOH:250 6-methyl-5-hepten-2-one; 1 KOH:250 hexahydropseudoionone; 1 KOH:250 6,10,14-trimethyl-2-pentadecanone; 1 KOH:360 methyl ethyl ketone; and 1 KOH:250 6-methyl-5-octen-2-one) in the process according to the invention results in less than 50% (respectively, 1.45% [average of two runs]:3.6%; 0.6%:2.5%; 0.6%:2.0%; 0.4%:1.6%; and 0.85% (average of two runs):1.9%) of unwanted diol by-products when compared to the diol by-products resulting from the same process with the same reactants and co-catalysts, but when the molar ratio of potassium catalyst-to-starting carbonyl was greater than 1:200 (respectively 1:31; 1:27; 1:24.5; 1:90; and 1:46). The reductions of between 52% and 76% in the resulting production of unwanted diol by-products based on differences between the molar ratios according to the present invention and molar ratios above those specified in our invention are very significant.

12. The desired product, the α -alkynol, is purified by distillation in order to separate the desired product from the by-products and the other components of the reaction mixture. The undesired by-product, the diol, remains in the residue of the distillation vessel, forms part of the waste products of the reaction, and has to be removed, involving further treatment.

13. It may be possible to recover the starting materials from the diol, but that would require further reactions, involving more equipment, more energy (higher temperature) and more catalyst, thus adding significant costs. However, the separation of the unreacted starting materials (the acetylene and the ketone) from the product is

15. Furthermore, I would like to point out that the small changes in the by-product yield (differences in the range of between 1.0% and 2.2%) can be measured very accurately, contrary to the assertions in the Office Action.

16. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: January 6, 2009



Dr. Werner Boprath